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CASE REPORT

Pleomorphic adenoma originating from submandibular heterotopic salivary gland tissue: A case report and review of the literature

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Summary We reported a case of pleomorphic adenoma originating from the submandibular heterotopic salivary gland tissue (HGST) of a 61-year-old man. Histologically, no lymphoid tissue was detected in the tumor. Immunohistochemical examination revealed that the luminal tumor cells of tubuloductal structures were positive for anti-α-amylase antibody. The outer tumor cells of tubuloductal structures and neoplastic myoepithelial cells were stained with K8.12, anti-vimentin antibody, and anti-S-100 protein antibody. No tumor cells reacted with anti-α-smooth muscle actin antibody. These suggest that the tumor cells may be derived from the ductal cells of the extranodal HSGT. No recurrence of the tumor was detected for seven years.

Introduction

Heterotopic salivary gland tissues (HSGTs) are rarely found in the hypophysis, external and middle ear, thyroglossal duct, mandible, tongue, thyroid and parathyroid glands, and cervical lymph node.[1–4] Although HSGT is identical with the normal salivary gland tissue and contains with serous, mucous, or mixed glandular acini, a neoplastic transformation of the cells from HSGT is extremely rare.[5–7] To the best our knowledge, 19 cases of benign tumors originating from HSGTs have been reported in the English literature.[2,3,6–17]

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In this paper, we present an additional case of pleomorphic adenoma originating from HSGT in the submandibular region.

A case report

A 61-year-old man was referred to the Kyushu University Dental Hospital for a painless swelling in the left submandibular region. He had noticed the nodular swelling in the left submandibular region about six weeks before visiting our hospital. The mass was 2.5×2.5 cm in size, smooth on the surface, movable and elastic hard. No tenderness was detected. Computed tomography scans showed a presence of a heterogeneously enhanced mass, which was apparently dissociated from the submandibular gland (Fig. 1). Ultrasonographic examination showed a lobular-structured hypoechoic mass without bottom echo. The tumor was completely encapsulated and dissociated from the platysma and the submandibular gland, and enucleated in a lump. No recurrence of the tumor was observed during seven-year follow-up period.

Pathologic findings

Histopathological findings of the sections of the enucleated tumor revealed pleomorphic adenoma (Fig. 2). Although a small number of infiltrated lymphocytes were detected, no lymphoid tissue was present in the sections. An immunohistochemical staining was performed on serial sections (4 μm in thickness) of the tumor by the avidin—biotin peroxidase complex (ABC) method (Vectastain ABC kit; Vector Laboratories, Burlingame, CA), using antibodies against α-amylase (Bio Pur AG, Budendorf, Switzerland; diluted 1:100), keratin no. 16, 13 (K8.12) (BioMakor, Rehovot, Israel; diluted 1:20), vimentin (DAKO, Glostrup, Denmark; diluted 1:25), S-100 protein (DAKO, Glostrup, Denmark; diluted 1:25), and α-smooth muscle actin (Chemicon International, Inc., USA; diluted 1:400). The luminal tumor cells of tubuloductal structures were positive for anti-α-amylase antibody. The outer tumor cells of the tubuloductal structure and neoplastic myoepithelial cells in the myxoid area were stained with K8.12, anti-vimentin antibody, and anti-S-100 protein antibody (Fig. 2). On the other hand, no tumor cells were stained with anti-α-smooth muscle actin antibody. When the tumor was stained with proliferating cell nuclear antigen (PCNA)—antibody (DAKO, Glostrup, Denmark; diluted 1:100), the mean PCNA index (total number of positive nuclei/total number of counted cells) was 4.1%.

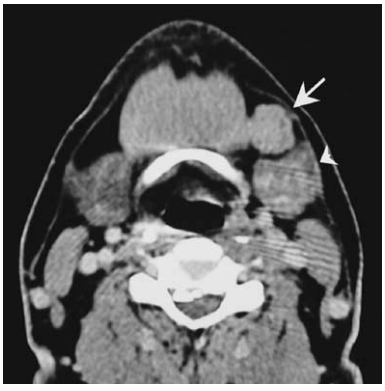

Figure 1 CT imaging. CT scan showed that the heterogeneously enhanced mass (arrow) was dissociated from the skin and the submandibular gland (arrow head).

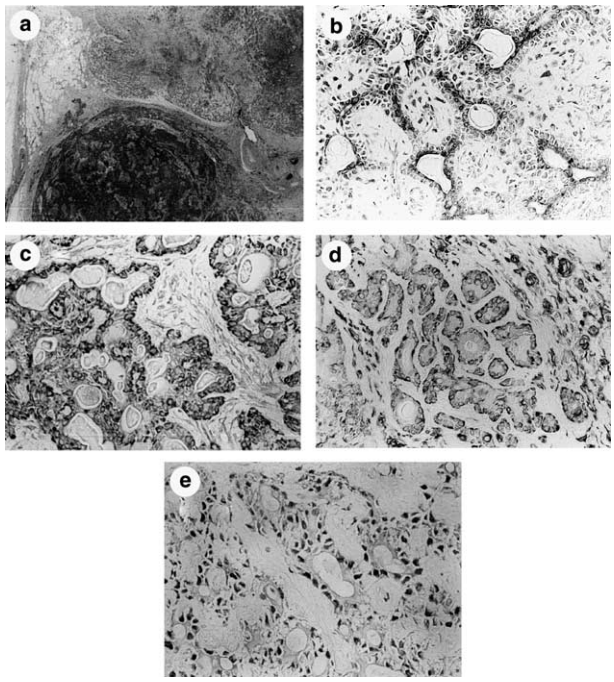

Figure 2 Histopathological and immunohistochemical findings. The tumor was completely encapsulated by fibrous connective tissue and fat tissue (a). No lymphoid tissue was present in the sections (H.E. magnification × 40). The tumor cells were stained with anti-α-amylase antibody (b; magnification ×200), K8.12 (c; magnification ×200), anti-vimentin antibody (d; magnification ×200), and anti-S-100 protein antibody (e; magnification ×200).

Discussion

We have presented a rare case of pleomorphic adenoma originating from the extranodal HSGT.

Pleomorphic adenoma can arise not only from salivary gland but also from other gland tissues such as skin appendages and the glands of breast or bronchia. It has been shown that some tumor cells from salivary glands are focally stained with anti-α-amylase antibody.[18] In our case, the luminal tumor cells of tubuloductal structures were stained with anti-α-amylase antibody, suggesting that the tumor cells may be originated from a salivary gland tissue.

The histogenesis of HSGT is explained by entrapment of salivary tissue during embryogenesis or heteroplastic changes of epithelial tissue.[2,3] An autopsy study demonstrated the presence of 100% intranodal HSGT in the parotid lymph nodes of 19 newborns.[1] Furthermore, a survey of lymph nodes in 257 neck dissection specimens showed that intranodal HSGT was detected in 31 patients (12.1%), and the majority of the HSGT was found in infra-auricular parotid lymph nodes, submandibular lymph nodes and superficial lateral cervical lymph nodes.[4] On the other hand, it was reported that extranodal HSGTs were detected in 110 cases of over 20,000 salivary gland lesions (less than 0.55%).[5] Neoplastic transformation of HSGT in the neck is extremely rare.[6,7] To the best our knowledge, excluding adenolymphoma, only 19 cases of benign salivary tumors originating from HSGTs in the neck have been reported (Table 1). Eighteen cases (95%) are pleomorphic adenomas, and one (5%) is an oncocytoma. An interesting finding is that 11 of the 19 cases (58%) are originated from extranodal HSGTs. Furthermore, neoplastic transformation from extranodal HSGT occurs more frequently at the upper part of the neck, although most extranodal HSGTs are present at the lower part of the neck.[3] Thus, the incidence of neoplastic transformation might be higher in extranodal HSGT in the upper neck than other HSGT in the neck.

The outer tumor cells of tubuloductal structures were stained with K8.12, anti-vimentin antibody and anti-S-100 protein antibody, but not with anti-α-smooth muscle actin antibody. These findings are consistent with those of pleomorphic adenomas originating from normal salivary gland tissues.[19] The tumor cells, therefore, may be derived from the ductal cells rather than myoepithelial cells of HSGT. The mean PCNA index in the present case

Table 1 Benign tumors of cervical heterotopic salivary gland tissues (excluding adenolymphoma)

Author	Year	Age	Sex	Side	Region	Diagnosis	Treatment
Pesavento and Ferlito[8]	1976	36	F	R	Upper part of anterior border of SCM	PA	Excision
Bothra et al.[9]	1977	50	F	L	One inch above sternoclavicular joint	PA	Excision
Mair et al.[10]	1978	40	M	L	Upper neck, level of hyoid	PA	Excision
Hulbert[11]	1978	41	F	L	Upper part of anterior border of SCM	PA	Excision
Singer et al.[2]	1979	61	M	R	Angle of mandible	PA	Excision
Zajtchuk et al.[12]	1982	32	F	L	Juglodigastric LN	PA	Excision
		30	F	?	Submandibular LN	PA	Excision
		35	F	?	Submandibular gland LN	Oncocytoma	Excision
Cotelingam and Gerberi[13]	1983	22	M	L	Upper part of anterior border of SCM	PA	Excision
Lind and Bang[3]	1983	11	F	R	Angle of mandible	PA	Excision
		62	M	L	Upper part of anterior border of SCM	PA	Excision
Rodgers et al.[7]	1991	14	M	R	Upper part of anterior border of SCM	PA	Excision
Evans and Rubin[14]	1991	11	F	L	LN below angle of mandible	PA	Excision
		15	M	R	LN below angle of mandible	PA	Excision
Surana et al.[6]	1993	9	F	L	LN at jugulodigastric region	PA	Excision
		12	F	R	LN at jugulodigastric region	PA	Excision
Tay and Howitt[15]	1995	50	M	L	Anterior border of the trapezius muscle	PA	Excision
Shinohara et al.[16]	1996	21	M	R	Parotid and submandibular LNs	PA	Excision
Ohsawa et al.[17]	2002	60	F	L	Submandibular region	PA	Excision
Present case		61	M	L	Submandibular region	PA	Excision

M: male, F: female, R: right, L: left, SCM: sternocleidomastoid, PA: pleomorphic adenoma, LN: lymph node.

(4.1%) was similar to that of pleomorphic adenomas originating from normal salivary gland tissues (3.4 ± 2.5%).[20] Therefore, the proliferating activity of the tumor cells in this case is the same as that in pleomorphic adenomas originating from normal salivary gland tissues. No recurrent sign was observed in a seven-year follow-up period.

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